Comparison of Microvasculature and Fundus Morphometric Features in High Myopia Regard to the Presence of Beta Zone Peripapillary Atrophy

Sema Tamer Kaderli[1], Aylin Karalezli[2], Ahmet Kaderli[3], Cansu Kaya[4], Sabahattin Sul[5]

ABSTRACT

Purpose: To compare the microvasculature and fundus morphometric features between the high myopic eyes with and without the beta zone peripapillary atrophy (β-PPA).

Methods: 38 eyes with high myopia (mean spherical equivalent (MSE) ≤- 6.00D) and 30 age-matched emmetropic eyes (- 1.00 ≤ MSE<+0.75D) were included in this prospective study. Two groups were created according to presence of β-PPA. Group 1 consisted of 26 eyes with normal OD, and group 2 consisted of 12 eyes with β-PPA. The vertical distance between the temporal superior and temporal inferior arterial arcade (VDA), the distance fovea to disc (DFD), and optical coherence tomography angiography (OCTA) were compared between the groups.

Results: The mean VDA and DFD were higher in group 2 than group1 and control group. The mean foveal avascular zone was larger and peripapillary VD was lower in all myopic eyes regardless of the presence of β-PPA in group 1 and 2 than the controls. (For FAZ p<0.001, p=0.002; for peripapillary VD p=0.049, p=0.004) The parafoveal VD in deep capillary plexus and VD of optic nerve head (ONH) were lower in group 2 than group 1. (For parafoveal VD p=0.015; for total disc VD p=0.008; for peripapillary VD p=0.017) There was a mild negative correlation between DFD and parafoveal VD and peripapillary VD in high myopic eyes. (r=-0.344, p=0.004; r=-0.365, p=0.002)

Conclusions: VD of ONH and parafovea was lower in high myopia with β-PPA. Decreased parafoveal and peripapillary VD was correlated with the elongation of the DFD.

Key words: High myopia, Vessel density, Distance fovea to disc, Optical coherence tomography angiography, Beta zone peripapillary atrophy..

INTRODUCTION

Myopia is the leading cause of refractive disorders that affects young people with an increased risk of blindness.[1] High myopia is clinically important to the individual patient and public health as it has become the main cause of visual field defects and central vision loss in the adult population in East Asia.[2]

Optical coherence tomography angiography (OCTA) allows non-invasive evaluation of retinal capillary network and microcirculation.[3] Previous studies have demonstrated the reproducibility of OCTA in optic nerve head and macular microvascular perfusion measurements.[4, 5] Furthermore, previous studies reported that the peripapillary vessel density (VD) was lower in myopic eyes compared to emmetropic eyes.[5-7]

Morphometric analysis of the anatomical features such as the vertical distance between the temporal superior and temporal inferior arterial arcade (VDA), the distance fovea to disc (DFD) have been previously investigated because they may be related to axial elongation.[8] Myopia is associated with typical changes of optic nerve head (ONH) structure, such as the development of peripapillary atrophy or focal lamina cribrosa defect. Regional vascular deficiency may increase vulnerability to optic nerve injury.[9-11] The aim of this study was to evaluate the quantitative features of fundus image and retinal microvasculature in high myopia and to compare the microvasculature and

1- MD, Mugla Education and Research Hospital, Ophthalmology Departmant, Mugla, Turkey

2- Prof., Mugla Sitki Kocman University, Ophthalmology Department, Mugla, Turkey

3- Assoc. Prof., Mugla Sitki Kocman University, Ophthalmology Department, Mugla, Turkey

4- MD, Mugla Sitki Kocman University, Ophthalmology Department, Mugla, Turkey

5- Assoc. Prof., Mugla Sitki Kocman University, Ophthalmology Department, Mugla, Turkey

Received: 16.12.2022
Accepted: 07.03.2023

J Ret-Vit 2023; 32: 179-186

DOİ: 10.37845/ret.vit.2023.32.30

Correspondence Adress:
Sema Tamer Kaderli
Mugla Education and Research Hospital, Ophthalmology Department, Mugla, Türkiye

Phone: +90 507 411 0129
E-mail: sematamerkaderli@hotmail.com

fundus morphometric features in high myopia regard to presence beta zone peripapillary atrophy.

MATERIALS AND METHODS

38 eyes of nineteen patients who were referred to retina department from November 2020 to February 2021 were included in this prospective study. All patients were informed of the study protocol, and written informed consent was collected. This study adhered to the principles of the Declaration of Helsinki. Approval from local ethics committee was obtained (Approval number:13/IX).

Cases with high myopia (mean spherical equivalent (MSE)≤-6.00D) without peripheral and macular pathology, DR and no history of prior treatment (e.g., laser photocoagulation, intravitreal injection) were included in the study. Cases with peripheral abnormalities (chorioretinal atrophy, lattice degenerative lessions), myopic maculopathy and history or symptoms of chorioretinal diseases (e.g.choroidal neovascularization) were excluded from the study.

All patients underwent a baseline ophthalmic examination that included slit-lamp examination, fundus examination, OCT, and OCTA. OCTA was used to evaluate the foveal avascular zone (FAZ), the superficial capillary plexus (SCP), deep capillary plexus (DCP), choriocapillaris plexus (CCP) and retinal nerve fiber layer thickness (RNFL). The patients were classified into two groups: group 1 included 26 eyes with normal OD and group 2 included 12 eyes with beta-zone peripapillary atrophy (β-PPA). The β-PPA was defined as the area without retinal pigment epithelium when evaluated by OCT slab.[12, 13] The axial length (AL) was measured by IOL Master 700 (Carl Zeiss, Meditec AG, Jena, Germany) in all patients.

OCTA using the split-spectrum amplitude-decorrelation angiography (SSADA) method is described in detail in previous studies.[14] The OCTA (RTVue; Optovue, Fremont, CA) database was recorded in all patients. The VD was automatically measured by the software installed in the OCTA scanner. The parafoveal regions of the ETDRS grid were used for the local examination of the VD for both the SCP and DCP. Flow area of the choriocapillaris layer was obtained at 1 mm radius areas, centered on the foveal avascular zone (FAZ). The scan area of 6 mm × 6 mm, centered on the fovea, was performed in this study. Peripapillary flow was validated by total disc and peripapillary VD was measured using a 4.5 × 4.5-mm scan that was centered on the ONH, as previously described.[15] The software automatically hangs a 2.0 mm diameter circle centered on the optic disc and determines the peripapillary area as a 1.0 mm-wide round annulus extending from the optic disc 2.0-mm circle. The "Auto All" function of the device, OCTA signal position was obtained and images with quality below 8/10 were excluded. In cases in which we were concerned inability of automatic layer splitting, the adjustment was applied manually. 30 age and sex matched emmetropic eyes (- 1.00 ≤ MSE< +0.75D) were also included as a control group in this study.

Widefield fundus photography with the Optos 200Tx (Optos, Dunfermline, United Kingdom) and California (Optos) systems was performed for each patient. The quantitative features (The vertical distance between the temporal superior and temporal inferior arter arcade (VDA), the distance between the OD and the fovea (DFD)) were measured on fundus photographs. The VDA and DFD on widefield fundus image in a highly myopic eye with normal optic disc was shown in Figure 1A, in a highly myopic eye with β-PPA in Figure 1B and in an emmetropic eye in Figure 1C. Peripheral areas of defocus, artifacts, and poor illumination were excluded. The linear measurements of fundus structures have to take into account the magnification by the optic media of the eye. For the correction of the magnification of the fundus images by the ocular optic media, we used the Bennett application of the Littmann formula as in previous studies.[16, 17]

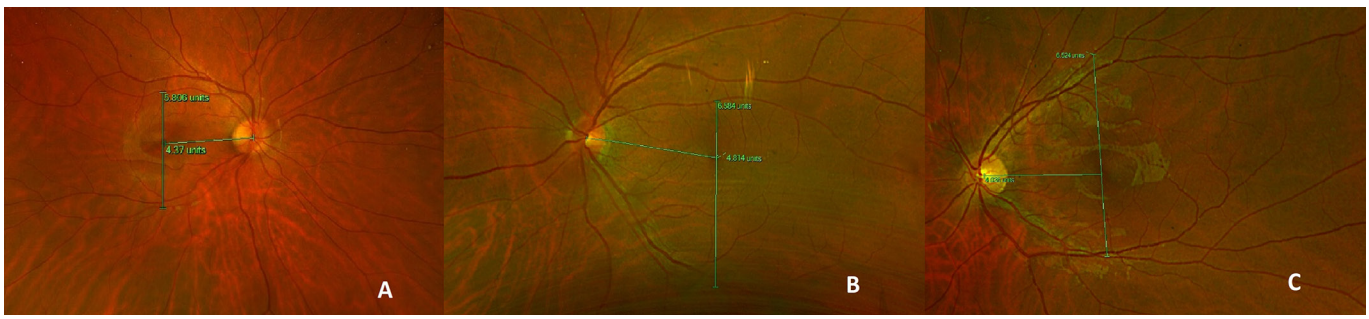

Figure 1: A. *The vertical distance between the temporal superior and temporal inferior arterial arcade and the distance fovea to disc on widefield fundus image in highly myopic eye with normal optic disc.* **B.** *In highly myopic eye with β-PPA* **C.** *In emmetropic eye.*

The SPSS 21.0 (SPSS, Inc, Chicago, IL) program was applied. Components that were quantitative in the form of analysis were examined by the Shapiro Wilk test for the normality hypothesis. Comparisons between categorical variables were estimated using contingency tables and chi-square test or Fisher's test, when necessary. The one-way analysis of variance (ANOVA) with post-hoc Bonferroni correction was used to evaluate the clinical characteristics, quantitative fundus image and OCTA parameters between the groups. Pearson's correlation analyses were used to examine the relationships between the morphometric fundus features, AL and OCTA parameters. A P value of lower than 0.05 was considered as statistically significant.

RESULTS

The clinical and demographic characteristics were summarized in table 1. There was no significant difference between the groups in terms of age, gender distribution, central macular thickness, and intraocular pressure. (p> 0.05 for all). (Table 1)

The RNFL thickness was significantly lower in group 2 than group 1 and control group. (p=0.012, p<0.001) The mean AL was significantly higher in group 2 and than the group1 and control group. (p=0.001, p<0.001) The MSE was significantly lower in group 2 than the other groups. (p=0.025, p<0.001) (Table 1) The AL was higher than 26 mm in 19 eyes of 38 eyes. In 16 of 19 eyes (84.2%) with an AL of less than 26mm, there was no β-PPA. The 9 eyes of 19 with higher than 26mm had β-PPA.

The quantitative fundus image and OCTA parameters were evaluated and the results are shown in table 2. The mean VDA and the mean DFD was significantly higher in group2 than group1 and control group. (For VDA p=0.107, p=0.008; for DFD p=0.015, p=0.004). The mean FAZ was larger in group1 and group 2 than in control eyes. No significant difference was obtained in terms of FAZ between group1 and group 2. (p=0.858) (Table 2) The mean parafoveal VD in DCP and VD of ONH (total disc and peripapillary VD) were lower in group 2 than group 1 and control eyes. (Table 2) There was no significant difference in terms of VD in SCP and CCP flow area between the groups. (Table 2) Representative OCTA images comparing FAZ and VD were shown in highly myopic eye with normal optic disc in Figure 2A, in highly myopic eye with β-PPA in Figure 2B and in an emmetropic eye in Figure 2C.

We evaluated the relation between features of fundus image and microvascular parameters detected by OCTA. No obvious correlation between VDA and parafoveal VD, optic nerve head VDs was noted in the study. There was a mild negative correlation between DFD and parafoveal VD and peripapillary VD in high myopic eyes. (r=-0.344, p=0.004; r=-0.365, p=0.002) (Table 3) There was a negative correlation between AL and peripapillary and parafoveal

Table 1: *Clinical and demographic characteristics.*

	Mean±SD						
	Group1	Group2	Control group	p	p^A	p^B	p^C
n	(n=13)	(n=6)	(n=15)				
Age (years)	29.73±12.88	36.00±13.10	32.93± 11.46	0.256	0.250	0.536	0.702
Sex (F/M)	10/3	4/2	12/3	0.639	-	-	-
n	(n=26)	(n=12)	(n=30)				
CCT, µm	549.69±33.27	539.41±35.84	544.70±26.75	0.623	0.612	0.820	0.872
CMT, µm	243.38 ± 30.73	239.91±39.10	268.86±17.37	**0.001**	0.931	**0.003**	**0.008**
IOP, mmHg	15.07±2.96	14.00 ±2.59	14.96 ±2.74	0.520	0.518	0.988	0.575
Axial Length, mm	25.42±1.16	26.65±1.24	23.16±0.39	**<0.001**	**0.001**	**<0.001**	**<0.001**
RNFL thickness, µm	107.84 ± 10.48	97.50 ±12.23	112.80 ±8.59	**<0.001**	**0.012**	0.164	**<0.001**
Spherical equivalent, D	-8.76±2.35	-10.16±3.32	0.01±0.44	**<0.001**	**0.025**	**<0.001**	**<0.001**

Group 1; high myopic eyes with normal optic disc, group 2; high myopic eyes with β zone peripapillary atrophy. SD; standard deviation, CCT; central corneal thickness, CMT; central macular thickness, IOP; intraocular pressure, RNFL; retinal nerve fiber layer, D; diopter.
P^A: Difference between group1 and group 2. p^B: Difference between group 1 and control group. p^C: Difference between group 2 and control group

Table 2: *Quantitative fundus image and OCTA features of the high myopia patients and the control group.*

	Mean ± SD				Posthocs		
	Group1 (n=26)	Group2 (n=12)	Control (n=30)	P value	p^A	p^B	p^C
VDA (unit)	6.96±0.52	7.56±0.98	6.83±0.64	**0.010**	0.107	0.799	**0.008**
DFD (unit)	4.18±0.50	4.62±0.51	4.15±0.29	**0.013**	**0.015**	0.596	**0.004**
FAZ (mm²)	0.286±0.105	0.279±0.091	0.196±0.03	**<0.001**	0.858	**<0.001**	**0.002**
VD in SCP(%)	54.02±3.9	52.43±4.4	52.68±2.1	0.100	-	-	-
VD inDCP(%)	58.83±6.3	53.86±6.5	59.86±6.1	**0.013**	**0.015**	0.700	**0.030**
VD of ONH (%) Total disc Peripapillary	 49.85±3.06 50.76±3.41	 46.41±4.3 46.53±6.92	 50.13±2.65 52.14±1.93	 **0.023** **0.010**	 **0.008** **0.017**	 0.642 0.059	 **0.018** **0.004**
CCP flow area (mm²)	2.220±0.120	2.159±0.127	2.155±0.13	0.117	-	-	-

Group 1: High myopic eyes with normal optic disc. Group 2: High myopic eyes with beta zone peripapillary atrophy.
VDA; the vertical distance between the temporal superior and temporal inferior arterial arcade, DFD; the distance between the fovea and optic disc dia; diameter, FAZ; Foveal avascular zone, VD; Vessel density, SCP; Superficial capillary plexus, DCP; Deep capillary plexus, ONH; Optic nerve head, SD; Standard deviation
P^A: Difference between group1 and group 2. p^B: Difference between group 1 and control group. p^C: Difference between group 2 and control group

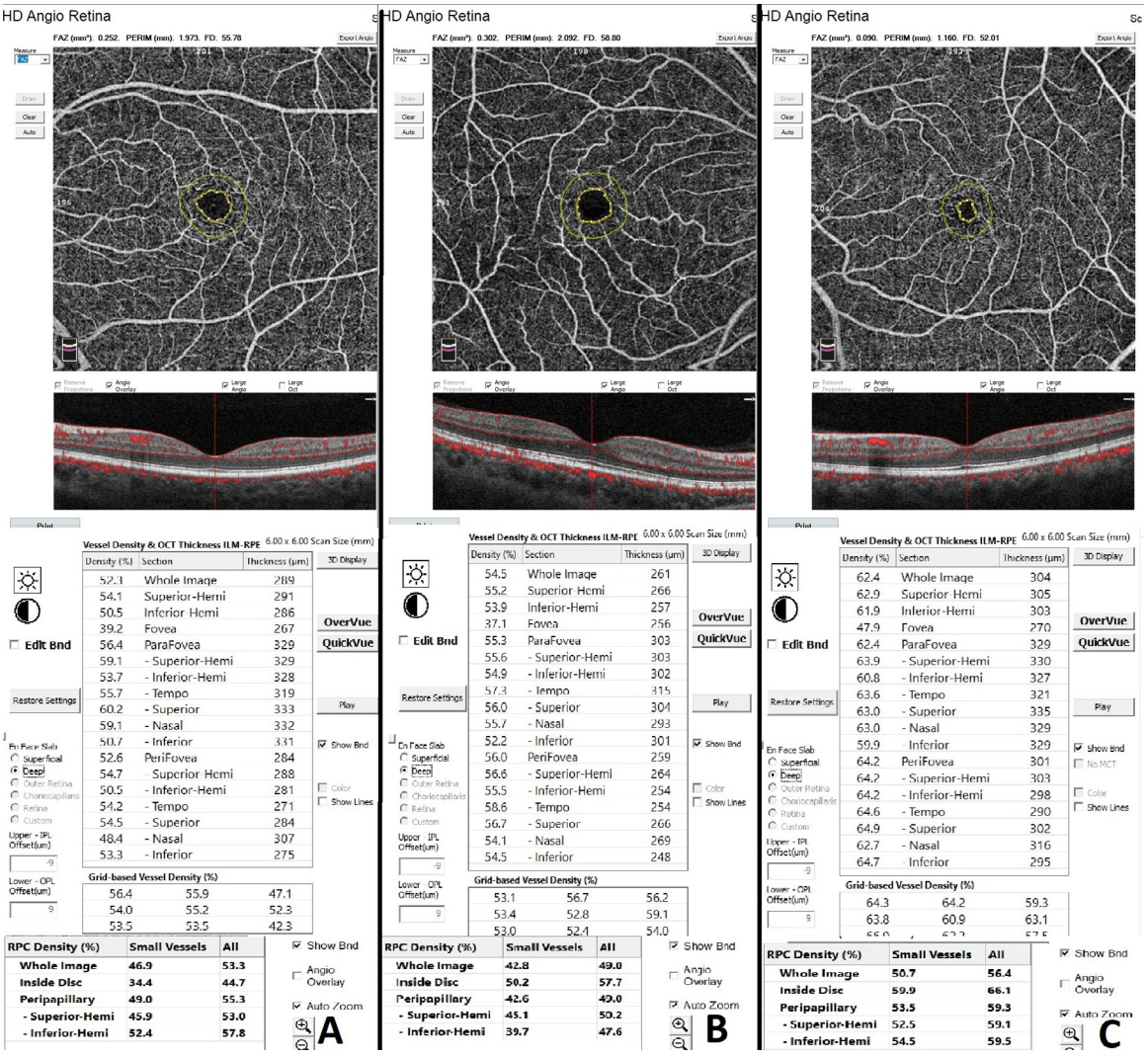

Figure 2: *Representative OCTA images comparing FAZ and VD of the groups* **A.** *In highly myopic eye with normal optic disc.* **B.** *In highly myopic eye with β-PPA* **C.** *In emmetropic eye.*

VDin DCP. The positive correlation was obtained between AL and FAZ (Table 3).

DISCUSSION

In this study, we attempted to compare the quantitative features of fundus image and retinal microvasculature in high myopia. We found that the VDs of ONH and the parafoveal VD in DCP were lower in myopic eyes with β-PPA. Furthermore, we identified that the mean VDA and DFD were significantly higher in these eyes. FAZ was larger in all myopic eyes than control group. Decreased peripapillary VD was correlated with the elongation of DFD and FAZ was correlated with AL.

Emmetropization is the modification of the length of the optical axis to the given cornea and lens after the end of the second year of life. Until the end of the second year of life, the eye develops spherically. Axial elongation is associated with a thinning of the retina and a decreased frequency of retinal pigment epithelium (RPE) cells in the retro-equatorial region, a choroidal and scleral thinning, beginning at the equator and being most marked at the macula. The increased AL may occur by the composition of additional bruch membrane (BM) in the retro equatorial area leading to a decreased RPE density and retinal thinning in that region. The enlargement of the globe is more tube-like than spherical. Previous histomorphometric studies have shown that DFD increases with longer axial length.[8, 18, 19] In high axial myopic eyes the elongation of DFD was due to the development and enlargement of peripapillary atrophy. In our study we found that the DFD was significantly larger in myopic eyes with β-PPA.

Previous studies have shown that the elongation of AL and the narrowing of the retinal vessel width in high myopia may also contribute to reduced density. The retinal dysfunction may be caused by compromise to the retinal vasculature, secondary to AL, which would seem to unavoidably stretch the retinal vasculature.[20-22] Yang et al reported that the significant correlation between the microvessel density and AL may also suggest that the global elongation may affect the retinal microvasculature.[23] Similar to their study we also found a negative correlation between AL and microvessel density of parafovea and peripapillary zone. Assessing the morphometric features of the fundus image was a unique point in our study. The 82% percentage of eyes with lesser than 26mm had not peripapillary atrophy. No obvious correlation was observed between AL and peripapillary atrophy in our study. However, VDs were found to be statistically significantly lower in both eyes with AL of more than 26mm and eyes with β-PPA. We concluded that if peripapillary atrophy exists, although the AL is shorter than 26mm, those eyes may be susceptible to ischemical damage in the future.

Table 3: *Correlations between OCTA parameters and quantitative fundus image features in the patients with high myopia*

	VDA (p-Value)	DFD (p-Value)	AL (p-Value)	FAZ (p-Value)	VD in SCP (p-Value)	VD inDCP (p-Value)	CCP (p-Value)	VD whole (p-Value)	Peripapillary VD (p-Value)
VDA	1								
DFD	0.361 (0.037)	1							
AL	0.237 (0.059)	0.260 (0.032)	1						
FAZ	-0.201 (0.101)	0.217 (0.075)	0.372 (0.002)	1					
VD in SCP	0.018 (0.886)	-0.197 (0.107)	-0.285 (0.018)	0.025 (0.840)	1				
VD in DCP	0.096 (0.434)	-0.344 (0.004)	-0.497 (0.001)	-0.207 (0.09)	0.683 (0.001)	1			
CCP	-0.062 (0.616)	0.037 (0.767)	-0.006 (0.963)	0.115 (0.351)	0.106 (0.392)	-0.065 (0.600)	1		
VD whole	0.053 (0.667)	-0.087 (0.478)	-0.294 (0.015)	0.062 (0.617)	0.323 (0.007)	0.315 (0.009)	0.171 (0.163)	1	
Peripapillary VD	0.102 (0.406)	-0.365 (0.002)	-0.468 (0.001)	-0.365 (0.002)	0.147 (0.232)	0.397 (0.001)	0.130 (0.292)	0.348 (0.004)	1

p-values are derived from Pearson's test. VDA; the vertical distance between the temporal superior and temporal inferior arterial arcade, DFD; diameter of fovea to disc, AL; axial length, FAZ; foveal avascular zone, SCP; superficial capillary plexus, DCP; deep capillary plexus, CCP; choriocapillar plexus flow area, VD; vessel density.

Jonas et al reported that VDA in eyes without macular BM defects was independent of axial length. Therefore the authors suggested that the BM in the whole macular region did not enlarge in axially elongated eyes without BM defects.[24] In another study it was reported that chorioretinal lesions consist of loss of RPE and macular BM defects. VDA was found to be increased in myopic eyes with chorioretinal atrophy, the authors suggested that this increase may be from BM openings.[25, 26] In our study we did not include the myopic eyes with chorioretinal atrophy. The VDA and AL were higher in myopic eyes with β-PPA.

DFD is an another important anatomical measurement of the posterior fundus and may be associated with other ocular disorders. It can be assumed that a postnatal enlarged DFD in highly myopic eyes can be associated with the stretching of the posterior fundus and thus an increased photoreceptor distance and thereby have a direct effect on the microvascular structure. This change in microvascular structure may be associated with the complications of myopia and visual acuity. Vurgese et al found that the axial myopic elongation leads to an enlargement of the globes mainly in its posterior segment, starting mostly at or behind the equator and being more pronounced the closer to the posterior pole.[27] Jonas et al found significant associations between the DFD and axial length and larger parapapillary zones.[28] In our study the DFD was significantly higher in myopic eyes with β-PPA. Furthermore, in these eyes, the RNFL thickness and parafoveal density were significantly lower than the other groups. The elongation of the DFD may conceivably lead to increased metabolic demands in retina due to parapapillary RNFL thinning, leading to a reduced parafoveal microvascular density. In myopic eyes where the peripapillary microvascular structure is interrupted, the retinal capillary network can not meet the metabolic demands with the increase in AL and DFD, and microvascular disorders start to occur in the parafoveal area. However, it is still difficult to illuminate whether the decreased VD was cause or consequence of the ocular structural changes based on this cross sectional study. Future longitudinal studies are required to broaden our understanding on this.

It is known that high myopia is associated with elongation of the eyeball, which creates a stretching effect on the ocular wall, including the sclera, choroid and retina. Under the effect of this stretching, the RNFL becomes thinner and restriction in peripapillary perfusion can be observed. [29] Previous studies have shown that parapapillary VD is negatively correlated with AL. Shimada et al. demonstrated a significant reduction in retinal blood flow in eyes with high myopia using quantitative methods and laser Doppler velocimetry. They also noted that the impaired retinal blood flow might have a role in the development of chorioretinal atrophy in high myopia. [30] Assuming that one of the consequences of this stretching effect may also affect the main retinal vessels, we investigated whether there is a difference in anatomical lengths between the arcades and DFD or whether this is related to microvascular circulation.

With the frequent use of OCTA in our daily practice, the number valuable studies conducted with OCTA on myopic eyes is increasing in recent years. These studies can provide an enlightening idea about the pathophysiology of various complications that especially damage the optic nerve and macular area. Piao et al reported that FAZ was larger in high myopic eyes and strongly correlated with acircularity and circularity indexes of FAZ in the high myopic eyes. [31] There are some hypotheses that have been offered for explaining FAZ expansion in myopic eyes that remain unclear. The retinal vascular structure dragging during myopia progression may decrease retinal blood flow and further result in variation in the FAZ size.

Previous studies demonstrated that the FAZ was significantly associated with optic nerve head tilt, which occurs during axial elongation.[31, 32] Another hypothesis is that overall macular thinning may cause decreased oxygen consumption, resulting in decreased retinal blood flow and increased FAZ area. He et al reported the reduced radial peripapillary VD and enlarged FAZ in high myopia.[33] They also found a correlation between the tilted disc ratio and retinal perfusion. They also found a lower tilted disc ratio in high myopic eyes and correlation between the tilted disc ratio and retinal perfusion. They observed no significant difference in terms of RNFL between emmetropic and myopic eyes. Similar to their results, we observed enlarged FAZ and decreased VD in peripapillary and parafoveal region in myopic eyes with β-PPA. However we did not find any differences in terms of FAZ between groups with high myopia.

Guo et al. reported that high myopia had a lower peripapillary VD when compared with emmetropia, mild and moderate myopia. Furthermore, they showed that the correlation of the parapapillary microvascular density with AL and RNFL thickness. However, they did not obtain any significant difference in parafoveal VD. [7] In our study, the VD in DCP was significantly lower in high myopia with β-PPA similar to previous other results.[21, 23]

This study was limited in lower sample sizes. The linear measurements of fundus structures have to take into account the magnification by the optic media of the eye. It may lead to inaccuracies in the measurements in absolute

size units. For the correction of the magnification of the fundus images by the ocular optic media, we used the Bennett application of the Littmann formula as in previous studies. In previous studies, the litmann formula was used in telecentric cameras such as Zeiss.[16] The lack of a similar study with Optos comparing magnification is another limitation of this study.

In conclusion, axial elongation led to a decrease in parafoveal and peripapillary vessel density because of an increase in the DFD (caused by the β-PPA). By contrast, the VDA in myopic eyes was independent of microvascular structure. It suggests that the elongation of DFD leads to decreasing parafoveal and optic nerve head VD in myopic eyes with β-PPA fitting with previous observations. The retinal microvascular structure may shed light on the underlying pathophysiology of myopia, prediction of complications and development of new treatments.

Ethical Review Board

Compliance with Ethical Standards:

No funding was received for this research.

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval from local ethics committee obtained (Approval number:13/IX).

Informed consent: Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Holden BA, Fricke TR, Wilson DA et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology 2016; 123:1036-42.
2. He M, Zeng J, Liu Y et al. Refractive error and visual impairment in urban children in southern china. Investigative ophthalmology & visual science 2004; 45:793-9.
3. Savastano MC, Lumbroso B and Rispoli M. In Vivo Characterization of Retinal Vascularization Morphology Using Optical Coherence Tomography Angiography. Retina 2015; 35:2196-203.
4. Wei E, Jia Y, Tan O et al. Parafoveal retinal vascular response to pattern visual stimulation assessed with OCT angiography. PloS one 2013; 8:e81343.
5. Wang X, Kong X, Jiang C et al. Is the peripapillary retinal perfusion related to myopia in healthy eyes? A prospective comparative study. BMJ open 2016; 6:e010791.
6. Chen Q, He J, Hua Y and Fan Y. Exploration of peripapillary vessel density in highly myopic eyes with peripapillary intrachoroidal cavitation and its relationship with ocular parameters using optical coherence tomography angiography. Clinical & experimental ophthalmology 2017; 45:884-893.
7. Guo Y, Sung MS and Park SW. Assessment of superficial retinal microvascular density in healthy myopia. International ophthalmology 2019; 39:1861-70.
8. Guo Y, Liu LJ, Tang P et al. Optic disc-fovea distance and myopia progression in school children: the Beijing Children Eye Study. Acta ophthalmologica 2018; 96:e606-e613.
9. Kim TW, Kim M, Weinreb RN et al. Optic disc change with incipient myopia of childhood. Ophthalmology 2012; 119:21-26 e21-23.
10. Samarawickrama C, Mitchell P, Tong L et al. Myopia-related optic disc and retinal changes in adolescent children from singapore. Ophthalmology 2011; 118:2050-2057.
11. Sawada Y, Araie M, Kasuga H et al. Focal Lamina Cribrosa Defect in Myopic Eyes With Nonprogressive Glaucomatous Visual Field Defect. Am J Ophthalmol 2018; 190:34-49.
12. Dai Y, Jonas JB, Huang H et al. Microstructure of parapapillary atrophy: beta zone and gamma zone. Invest Ophthalmol Vis Sci 2013; 54:2013-8.
13. Jonas JB, Jonas SB, Jonas RA et al. Parapapillary atrophy: histological gamma zone and delta zone. PLoS One 2012; 7:e47237.
14. Spaide RF, Klancnik JM, Jr. and Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA Ophthalmol 2015; 133:45-50.
15. Khairallah M, Abroug N, Khochtali S et al. Optical Coherence Tomography Angiography in Patients with Behcet Uveitis. Retina 2017; 37:1678-91.
16. Knaapi L, Aarnisalo E, Vesti E and Leinonen MT. Clinical verification of the formula of Bennett et al. (1994) of determining the size of retinal features by fundus photography. Acta ophthalmologica 2015; 93:248-52.
17. Bennett AG, Rudnicka AR and Edgar DF. Improvements on Littmann's method of determining the size of retinal features by fundus photography. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie 1994; 232:361-7.
18. Jonas JB, Wang YX, Zhang Q et al. Macular Bruch's Membrane Length and Axial Length. The Beijing Eye Study. PloS one 2015; 10:e0136833.
19. Jonas JB, Ohno-Matsui K and Panda-Jonas S. Myopia: Anatomic Changes and Consequences for Its Etiology. Asia-Pacific journal of ophthalmology 2019; 8:355-359.
20. Li H, Mitchell P, Rochtchina E et al. Retinal vessel caliber and myopic retinopathy: the blue mountains eye study. Ophthalmic epidemiology 2011; 18:275-80.
21. Li M, Yang Y, Jiang H et al. Retinal Microvascular Network and Microcirculation Assessments in High Myopia. American journal of ophthalmology 2017; 174:56-67.
22. Lim LS, Cheung CY, Lin X et al. Influence of refractive error

and axial length on retinal vessel geometric characteristics. Investigative ophthalmology & visual science 2011; 52:669-78.

23. Yang Y, Wang J, Jiang H et al. Retinal Microvasculature Alteration in High Myopia. Investigative ophthalmology & visual science 2016; 57:6020-30.
24. Jonas JB, Weber P, Nagaoka N and Ohno-Matsui K. Temporal Vascular Arcade Width and Angle in High Axial Myopia. Retina 2018; 38:1839-47.
25. Jonas JB, Ohno-Matsui K, Spaide RF et al. Macular Bruch's membrane defects and axial length: association with gamma zone and delta zone in peripapillary region. Investigative ophthalmology & visual science 2013; 54:1295-302.
26. Ohno-Matsui K, Jonas JB and Spaide RF. Macular Bruch Membrane Holes in Choroidal Neovascularization-Related Myopic Macular Atrophy by Swept-Source Optical Coherence Tomography. American journal of ophthalmology 2016; 162:133-139 e131.
27. Vurgese S, Panda-Jonas S and Jonas JB. Scleral thickness in human eyes. PloS one 2012; 7:e29692.
28. Jonas RA, Wang YX, Yang H et al. Optic Disc-Fovea Distance, Axial Length and Parapapillary Zones. The Beijing Eye Study 2011. PloS one 2015; 10:e0138701.
29. Leung CK, Mohamed S, Leung KS et al. Retinal nerve fiber layer measurements in myopia: An optical coherence tomography study. Investigative ophthalmology & visual science 2006; 47:5171-6.
30. Shimada N, Ohno-Matsui K, Harino S et al. Reduction of retinal blood flow in high myopia. Graefes Arch Clin Exp Ophthalmol 2004; 242:284-8.
31. Piao H, Guo Y, Zhang H et al. Acircularity and circularity indexes of the foveal avascular zone in high myopia. Sci Rep 2021; 11:16808.
32. Sung MS, Lee TH, Heo H and Park SW. Association Between Optic Nerve Head Deformation and Retinal Microvasculature in High Myopia. Am J Ophthalmol 2018; 188:81-90.
33. He J, Chen Q, Yin Y et al. Association between retinal microvasculature and optic disc alterations in high myopia. Eye 2019; 33:1494-503.